Immunodiagnostic Modifications
Including, but not limited to: lateral flow, ELISA

Guidance Detail - Immunodiagnostics

Category	Component	Type of change	Level of Change				Study Design - Testing Requirements on Separate Tab
			Level 3	Level 2	Level 1	Internal Info	
Assay Reagents	Critical Components including Antibodies (monoclonal, polyclonal, recombinant proteins), Calibrants, Gold Colloidal, and Antigen Conjugate in Competitive Assays	Modification of antibodies, calibrant or gold colloid, or antigen conjugate: 1. Polyclonal antibody - new animal species 2. Monoclonal antibody - replacement or addition or new clone 3. Modification to conjugation chemistry for the primary antibody (e.g. antibody-HRP conjugations) or primary antigen conjugation in competitive ELISAs 4. Gold colloid - changing the size or shape 5. Calibrant (what the kit is balanced to during the manufacturing process, such as standards in ELISA)- changing the material or the nature of the material (ex. peanut butter to peanut flour or Aflatoxin standard in Acetonitrile to Mycotoxin Reference Material)	X				1. Selectivity - full study 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability 5. Lot-to-lot consistency 5. Independent laboratory study
		Calibrant - changing from a reference material/standard to non-reference material/standard (ex. certified reference material to store-bought material)		X			1. Calibration study if applicable 2. Matrix study & LOD/LOQ if applicable 3. Product stability
		Modification of an existing antibody without modification of the recognition site (binding site). Change in animal for polyclonal antibody (same species).		X			1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability
		Change in the concentration of antibody or change in gold colloidal reducing agent. This does not include concentration adjustments needed to meet established product quality specifications as part of standard manufacturing process.		X			1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability
		Change in reaction pH @ antibody/antigen step (>0.5). NOTE: major changes in pH (e.g. moving from acidic to basic) would be a level 3 modification		X			1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable
		Change in reaction volume @ antibody/antigen step (Identical concentration)		X			1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable
		Change in supplier of critical component (ex. new supplier of the same monoclonal antibody)				X	1. Internal lot-to-lot consistency
		Polyclonal antibody - new bleeds from same animal(s)				X	1. Internal lot-to-lot consistency
	Other Reagents including alkaline phosphatase, peroxidase, wash buffer, dye, substrate, non-critical (see above) conjugate, kit controls, stop solution, extraction buffer, etc.	Replacement, addition or change in concentration of active ingredient (ex. new active ingredient to cause color change during substrate reaction). This does not include concentration adjustments needed to meet established product quality specifications as part of standard manufacturing process.		X			1. Matrix study & LOD/LOQ if applicable 2. Product or component stability 3. Lot-to-lot consistency If data from the new process falls outside of performance claims (within method developers tolerance), change must be evaluated as a level 3 modification.
		Modification of conjugation chemistry (e.g. secondary antibody conjugations)		X			1. Matrix study & LOD/LOQ if applicable 2. Product or component stability 3. Lot-to-lot consistency
		Replacement, addition or change in concentration of supporting ingredient (ex. new preservative, salt, or phosphate buffer). This does not include concentration adjustments needed to meet established product quality specifications as part of standard manufacturing process.				X	1. Internal lot-to-lot consistency 2. Internal stability data - expected for new preservatives
		Modification of the active ingredient supplier of the raw material				X	1. Internal lot-to-lot consistency
		Modification of the supporting ingredient supplier of the raw material				X	1. Internal verification of product quality
Other Physical Materials	Antibody support (microplates, cones, latex, membranes, etc.)	Modification of the nature of the material of the capture medium (ex. changing from plastic to latex, changing plastics)	X				1. Selectivity - full study 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability 5. Lot-to-lot consistency 6. Independent laboratory study
		Modification of the capture medium (e.g. lateral flow membrane or microwell) size or shape		X		X	Discuss with your AOAC consultant to determine whether the change is a level 2 or internal information. Level 2: 1. Matrix study & LOD/LOQ if applicable 2. Robustness Internal Info: 1. Internal lot to lot consistency
		Modification of the material of the capture medium with same intended properties				X	1. Internal lot to lot consistency
	Other Physical Materials	Modification to the containers used to house kit components (lateral flow cassette, barrettes, plastic to glass ...)				X	1. Internal lot to lot consistency
		Modification to single-use kit components that do not house kit components (test tubes, mixing tubes, single-use pipettes..)				X	1. Internal verification of product quality
		Modification of the capture medium supplier (e.g. lateral flow membrane or microwell)				X	1. Internal lot to lot consistency
		Change in container material supplier (e.g. lateral flow cassette, barrettes)				X	1. Internal verification of product quality
Instrumentation	Hardware (ex. Readers, heat blocks, automation in testing)	Add a new instrument, visual option or automation		X			1. Selectivity - subset 2. Matrix study & LOD/LOQ if applicable 3. Instrument variation study - only required for new proprietary readers
		Physical modifications to the hardware with impact on data acquisition or interpretation		X			1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable
		Physical modifications to the hardware with no impact on data acquisition or interpretation				X	1. Internal verification of product quality
	Firmware (programed into the hardware) or Software (programed into the computer/processing for analysis)	Changes with impact on performance claims (cut-off, type of regression, calibration curve optimizations where product claims are changed)	X				1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Independent laboratory study
		Changes without impact on the claims (traceability, installation, bug fixes, minor calibration curve optimizations where performance claims are still met within AOAC specifications)				X	1. Internal verification of product quality
Method Workflow	Enrichment for microbiology methods OR extraction procedure for chemistry methods	Adding a new enrichment, adding a new extraction, adding or removing a supplement, or shortening enrichment or extraction time compared to original range	X				1. Selectivity - Micro: perform full inclusivity + 10 exclusive organisms (for blind coding). Subset must be chosen in collaboration with AOAC consultant. Chemistry: perform full study. This includes analytes, cross-reactors and potential interferents for chemistry. 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Robustness - may be required depending on the change and robustness parameters tested in the original study 5. Independent laboratory study

		Replacement, addition or change in concentration (for non-titrated reagents) or activity level (for titrated reagents) of proprietary media active ingredient or extraction/dilution solution active ingredient (ex. inhibitors, selective agents, growth enhancer, chemical responsible for extracting analyte)	X				1. Selectivity - Micro: perform full inclusivity + 10 exclusive organisms (for blind coding). Subset must be chosen in collaboration with AOAC consultant. Chemistry: perform full study. This includes analytes, cross-reactors and potential interferents for chemistry. 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Independent laboratory study
		Lengthening enrichment or extraction time outside of original range		X			1. Matrix study & LOD/LOQ if applicable
		Microbiology methods: Change in dilution ratio or increase in test portion size with the same dilution ratio		X			1. Matrix study - Test all matrixes affected by new procedure
		Microbiology methods: Decrease in test portion size with the same dilution ratio (assuming the test portion size does not go smaller than the reference method portion size)			X		Any changes to instructions or literature would follow standard editorial level 1 modification process.
		Chemistry methods: Change in dilution ratio or test portion size		X			1. Matrix study & LOD/LOQ if applicable - Test all matrixes affected by new procedure.
		Replacement, addition or change in concentration of proprietary media supporting ingredient or extraction/dilution solution supporting ingredient (ex. preservatives, buffer changes) without impact on performance claims.				X	1. Internal selectivity 2. Internal lot to lot consistency data
		A change to the supplier of an active ingredient in a proprietary media or extraction/dilution solution				X	1. Internal lot to lot consistency
		A change to the supplier of a supporting ingredient in a proprietary media or extraction/dilution solution				X	1. Internal verification of product quality
	Changes to method steps, not related to enrichment or extraction	Changes to method incubation - time or temperature change, volume (with same final concentration)	X	X			Discuss with your AOAC consultant to determine whether the change is a level 2 or 3 change. 1. Selectivity - subset 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability 5. Lot-to-lot consistency 6. Independent laboratory study - for level 3
		Other changes to method steps	X	X	X	X	Discuss with your AOAC consultant to determine level of change.
Kit production	Antibody or Gold Colloidal	Modification of the antibody or gold colloidal production process with changes to performance claims (new column supplier, new media for hybridomas, polishing antibodies, etc.)	X				1. Selectivity - full 2. Calibration study if applicable 3. Matrix study & LOD/LOQ if applicable 4. Product stability 5. Lot-to-lot consistency 6. Independent laboratory study
		Modification of the antibody or gold colloidal production process without changes to performance claims (new column supplier, new media for hybridomas, polishing antibodies, etc.)				X	1. Internal lot to lot consistency
	Primary kit and supporting components	Modification/Optimization of the production process including kit or supporting components, not including antibodies or gold colloidal (batch size, rate, coating time, drying, homogenization, etc.)				X	1. Internal verification of product quality
	Production site and equipment	Adding a new production site with new equipment			X (Non-ISO 9001)	X (ISO 9001)	Non-ISO 9001 accredited manufacturing facilities: lot-to-lot consistency data - 3 lots of new + 1 lot of old tested with 1 matrix across analytical range. ISO 9001 accredited facilities: Internal lot-to-lot consistency data is expected. If data from the new process falls outside of the performance claims (within method developers tolerance), change must be reported to AOAC as a level 2 modification.
		Moving existing equipment to a new production site (new address)				X	1. Internal verification of product quality
		New equipment at same production site				X	1. Internal verification of product quality
		New equipment or site for supplier				X	1. Internal verification of product quality
Matrix claims	Extensions with existing methods	Adding a matrix group to matrix claims. Matrix groups may include: environmental sample, food, or cannabis.		X			1. Calibration study if applicable (ex. matrix matched standards) 2. Matrix study & LOD/LOQ if applicable - Test all matrixes that will be added to the claim. 3. Independent laboratory study - 1 matrix study for every 5 tested in the matrix study above.
		Adding a new matrix that exceeds the requirement of an independent laboratory performing 1 matrix study for every 5 claimed		X			1. Calibration study if applicable (ex. matrix matched standards) 2. Matrix study & LOD/LOQ if applicable - Test all matrixes that will be added to the claim. 3. Independent laboratory study - 1 matrix study for every 5 tested in the matrix study above.
		Adding a new matrix that does not exceed the requirement of an independent laboratory performing 1 matrix study for every 5 claimed		X			1. Calibration study if applicable (ex. matrix matched standards) 2. Matrix study & LOD/LOQ if applicable- Test all matrixes that will be added to the claim. 3. Independent laboratory study - 1 matrix study for every 5 tested in the matrix study above.
	Extensions with new methods	Adding a new matrix with change to the enrichment or extraction method protocol	X	X			Follow guidelines above in 'method workflow' section and 'matrix claim-extensions with existing methods' section. Perform all relevant test requirements.
	Matrix Removal	Removing a matrix from the claim			X		Any changes to instructions or literature would follow standard editorial level 1 modification process. See editorial changes to document section. If a matrix is removed due to poor performance, the limitation must be placed in the IFU.
Changes to Quality Control	Changes to QC procedure	Changes to QC procedure			X (Non-ISO 9001)	X (ISO 9001)	Non-ISO 9001 manufacturing facilities: At annual renewal, send updated QA/QC summary procedure. ISO 9001 manufacturing facilities: Follow appropriate ISO 9001 steps for changes in QC procedures. AOAC should always have your updated ISO 9001 certificate. Submit updated ISO 9001 certificate at annual renewals.
Shelf life extension	ISO 9001 Companies	Shelf life extension			X (Non-ISO 9001)	X (ISO 9001)	Non-ISO 9001 manufacturing facilities: At annual renewal, submit shelf life extension data to AOAC. ISO 9001 manufacturing facilities: Follow appropriate ISO 9001 steps for changes in shelf life. AOAC should always have your updated ISO 9001 certificate. Submit updated ISO 9001 certificate at annual renewals.
Editorial changes to documents (IFU, labels, packaging, etc.) with AOAC PTM mark	Editorial changes unrelated to anything above	Editorial change with immediate certificate update needed (ex. re-branding)			X		Level 1 modification must be done before or at time of new document release. A level 1 modification fee will be charged.
		Editorial change with either no certificate updates needed or delayed certificate updates needed			X		Level 1 modification can be submitted with annual renewal. Only the annual renewal fee will be charged.
Method modifications that are not covered by any other section of this document.			X	X	X	X	Discuss with your AOAC consultant to determine level of change.